REMARKS

Applicants have amended claims 37-48 and 51-57. A marked-up copy of the claims is attached. Claims 37-57 remain pending. Support for the amended claims can be found throughout the specification as filed. See, for instance, page 4, lines 3-8, page 5, lines 3-24 and Examples 1-5. These amendments obviate the product of nature and written description rejections on pages 2-3 of the office action. Applicants also provide a declaration from Dr. Richard Smith. The office action is addressed in greater detail below.

The claims are definite

Several phrases were rejected as being indefinite on page 4 of the office action. Applicants respectfully traverse this rejection.

For definiteness, a claim need only reasonably apprise those skilled in the art of the utilization and scope of the invention. *Hybritech, Inc. v. Monoclonal Antibodies,* 231 USPQ 81, 94-95 (1986). Words are to be given their plain meaning as understood by the person of ordinary skill in the art, particularly given the limitations of the English language. *See* MPEP §§ 707.07(g); 2111.01 (August 2001). Claims are to be given their broadest reasonable interpretation consistent with applicants' specification. *See* MPEP § 2111 (August 2001). In sum, in order to reject the claims on definiteness grounds, it is incumbent on the examiner to show how and why the skilled person

having applicants' specification would not be apprised of the invention by the language-at-issue.

Turning to the specific rejections, item 4a has been corrected by amendment. Item 4b concerns chemically reactive amino acids. The meaning of this phrase is explained on page 4 of the specification and page 8 of the response filed December 18, 2001. Because the phrase is in the plural, as amended, at least 2 chemically reactive amino acid residues would be altered. The SCRs identified in Item 4c refers to any one of the SCRs of CR1, which have long been known to the skilled person. See pages 2-3 of the specification. Finally, with regard to item 4d, claim 48 has been amended to recite "non-essential," which is explained in the specification at page 5. In view of the foregoing, applicants submit that the claims are immediately understood by the skilled person, and therefore the rejections should be withdrawn.

Double patenting

On pages 5-6 of the office action, the examiner rejected claims 37, 51, and 57 on double patenting grounds over U.S. Patent No. 5,833,989. In making the rejection, the examiner did not consider the previous recitation that a mature SCR3 was not within the claims. Applicants have replaced the previous recitation with the phrase "having only a partial SCR3 sequence," which will distinguish mature SCR3 as effectively as the examiner's suggested "consisting of" transition phrase, but without limiting the claim in other manners. Applicants therefore request withdrawal of the rejection.

The claimed invention is not taught by Fearon

On pages 6-7 of the office action, the examiner rejected claims 37, 39 and 51-57 as anticipated by Fearon. On page 7, first full paragraph, the examiner states that Fearon discloses CR1 amino acids 125-191, which represent SCR3. Applicants respectfully traverse this rejection.

Applicants note that in order to reject a claim under 35 USC § 102, the examiner must demonstrate that each and every claim term is contained in a single prior art reference. *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 18 USPQ2d 1001, 1010 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 90 (Fed. Cir. 1986); *see also* MPEP § 2131 (August 2001). Claim terms are to be given their plain meaning as understood by the person of ordinary skill in the art, particularly given the limitations of the English language. *See* MPEP §§ 707.07(g); 2111.01 (August 2001). Claims are to be given their broadest reasonable interpretation consistent with applicants' specification. *See In re Zletz*, 13 USPQ2d 1320, 1322 (Fed Cir. 1989) (holding that claims must be interpreted as broadly as their terms reasonably allow); MPEP § 2111 (August 2001).

Not only must the claim terms, as reasonably interpreted, be present, an allegedly anticipatory reference must enable the person of ordinary skill to practice the invention as claimed. Otherwise, the invention cannot be said to have been already within the public's possession, which is required for anticipation. *See Akzo, N.V. v. U.S.I.T.C.*, 1 USPQ2d 1241, 1245 (Fed. Cir. 1986); *In re Brown*, 141 USPQ 245, 249 (CCPA 1964).

As applied by the examiner, Fearon discloses a complete SCR3. The instant claims, by their terms, cannot cover a complete SCR3, but rather only polypeptides having a partial SCR3, and that partial SCR3 must include (a) amino acids 6-11 of SEQ ID NO: 1 and/or (b) amino acids 11-20 of SEQ ID NO: 1. Such a polypeptide is nowhere disclosed in Fearon. See Dr. Richard Smith's declaration. Applicants therefore submit that Fearon cannot anticipate the claims and that the rejection should be withdrawn.

The claims invention is not taught by the combination of Fearon and Capon

On page 8 of the office action, the examiner rejected claims 48-50 as obvious over Fearon in view of Capon. Fearon was applied as before. The examiner admits that Fearon does not disclose the creation of chimeric proteins. Capon was cited for disclosing chimeric proteins comprising a plasma protein and a protein of interest. Applicants respectfully traverse this rejection.

At the outset, applicant(s) note that the examiner must show all of the recited claim elements in the combination of references that make up the rejection. When combining references to make out a *prima facie* case of obviousness, the examiner is obliged to show by citation to specific evidence in the cited references that (i) there was a suggestion/motivation to make the combination and (ii) there was a reasonable expectation that the combination would succeed. Both the suggestion/motivation and reasonable expectation must be found within the prior art, and not be gleaned from applicants' disclosure. *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991); *In re Dow*

Chemical Co., 5 USPQ2d 1529, 1531 (Fed. Cir. 1988); *W.L. Gore v. Garlock, Inc.*, 220 USPQ 303, 312-13 (Fed. Cir. 1983) (holding that is improper in combining references to hold against the inventor what is taught in the inventor's application); *see also* MPEP §§ 2142-43 (August 2001). Thus, the examiner must provide evidentiary support based upon the contents of the prior art to support all facets of the rejection, rather than just setting forth conclusory statements, subjective beliefs or unknown authority. *See In re Lee*, 277 F.3d 1338, 1343-44 (Fed. Cir. 2002).

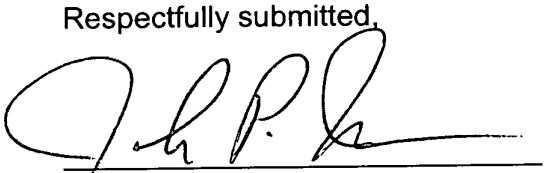
When an examiner alleges a *prima facie* case of obviousness, such an allegation can be overcome by showing that (i) there are elements not contained in the references or within the general skill in the art, (ii) the combination is improper (for example, there is a teaching away or no reasonable expectation of success) and/or (iii) objective indicia of patentability exist (for example, unexpected results). *See U.S. v. Adams*, 383 U.S. 39, 51-52 (1966); *Gillette Co. v. S.C. Johnson & Son, Inc.*, 16 USPQ2d 1923, 1927 (Fed. Cir. 1990); *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve*, 230 USPQ 416, 419-20 (Fed. Cir. 1986).

The limitations of Fearon are described above. Fearon concerns a complete SCR3, whereas the claimed invention does not. The deficiencies of Fearon are not rectified by Capon. Capon concerns proteins that are wholly distinct from CR1, and Capon does not rectify the primary deficiency of Fearon, namely that there is no disclosure of a partial SCR3 in either reference. See Dr. Smith's declaration. Accordingly, Fearon and Capon do not render the claims obvious, and thus the rejection should be withdrawn.

Request

Applicants submit that the claims are in condition for allowance, and respectfully request favorable consideration to that effect. The examiner is invited to contact the undersigned at (202) 912-2000 should there be any questions.

Respectfully submitted,



July 12, 2002

John P. Isacson
Attorney for Applicant
Reg. No. 33,715


26633

Heller Ehrman White & McAuliffe LLP
1666 K Street, N.W., Suite 300
Washington, D.C. 20006-4004
Telephone: (202) 912-2777
Facsimile: (202) 912-2020

Marked-up Copy of Amended Claims

37. (Four times amended) **[A] An SCR3 derivative** polypeptide **having only a partial SCR3 sequence , wherein the SCR3 derivative [comprising] comprises** a 6 to 23 amino acid portion of SEQ ID NO: 1, **and** wherein the **SCR3 derivative** polypeptide has at least one amino acid sequence selected from the group consisting of:

(a) amino acids 6-11 OF SEQ ID NO: 1, and

(b) amino acids 11-20 of SEQ ID NO: 1 **[, wherein the isolated polypeptide does not comprise a mature short consensus repeat-3]**.

38. (Twice amended) The **SCR3 derivative** polypeptide according to claim 37, further comprising a cysteine residue at the carboxyl terminus and the amino terminus of the polypeptide, thereby providing a capability to form a cyclic polypeptide via formation of a disulfide bond.

39. (Three times amended) The **SCR3 derivative** polypeptide according to claim 37, further comprising a chemically reactive amino acid residue located at least one position selected from the group consisting of the carboxyl terminus and the amino terminus of the polypeptide.

40. (Twice amended) The **SCR3 derivative** polypeptide according to claim 39, wherein the chemically reactive amino acid residue is derivatized or derivatizable.

41. (Twice amended) The **SCR3 derivative** polypeptide according to claim 40, wherein the terminal amino acid residue is cysteine derivatized with S-(2-pyridyl) dithio.

42. (Twice amended) The **SCR3 derivative** polypeptide according to claim 37, wherein the polypeptide is altered to remove chemically reactive amino **[acids] acid residues**.

43. (Four times amended) A multimeric **SCR3 derivative** polypeptide **having only a partial SCR3 sequence, wherein the SCR3 derivative polypeptide comprises [comprising]** at least two polypeptide constituents that comprise a 6 to 23 amino acid portion of SEQ ID NO: 1, **and** wherein the polypeptide constituents have at least one amino acid sequence selected from the group consisting of:

(a) amino acids 6-11 OF SEQ ID NO: 1, and

(b) amino acids 11-20 of SEQ ID NO: 1 , wherein the polypeptide constituents do not comprise a mature short consensus repeat-3 and the polypeptide constituents are linked to a core structure.

44. (Twice amended) The multimeric **SCR3 derivative** polypeptide according to claim 43, wherein the core structure comprises a derivative of lysine.

45. (Amended) The multimeric **SCR3 derivative** polypeptide according to claim 43, wherein the core structure is $(lys)_4(lys)_2$ lys ala or Tris (aminoethyl) amine and 1,2,4,5 benzene tetracarboxylic acid.

46. (Amended) The multimeric **SCR3 derivative** polypeptide according to claim 43, wherein the multimeric polypeptide comprises two to eight SCR3-derived polypeptides.

47. (Amended) The multimeric **SCR3 derivative** polypeptide according to claim 43, which comprises $(Lys)_4$ $(Lys)_2$ Ala-OH) linked through N-(ε-thiopropionyl) linkers that are disulfide bonded to cysteine thiol of the polypeptide SGGRKVFELVGEPSIYC.

48. (Four times amended) A chimeric polypeptide comprising a host protein and **as** an insert **an SCR3 derived** polypeptide **having only a partial SCR3 sequence, wherein the SCR3 derivative polypeptide comprises [comprising] comprises** a 6 to 23 amino acid portion of SEQ ID NO: 1, wherein the **SCR3 derived** polypeptide has at least one amino acid sequence selected from the group consisting of:

(a) amino acids 6-11 of SEQ ID NO: 1, and

(b) amino acids 11-20 of SEQ ID NO: 1,

wherein the **[insert]** **SCR3 d rived** polypeptide is inserted in**to** a **non-essential** region of the host protein **[, and the insert polypeptide does not comprise a mature short consensus repeat-3]**.

51. (Twice amended) The SCR3 **[-derived]** **derivative** polypeptide according to claim 37, wherein the SCR3 **[-derived]** **derivative** polypeptide is selected from the group consisting of:

linear CNPGSGGRKVFELVGEPSIYC (SEQ ID NO: 4);

cyclic CNPGSGGRKVFELVGEPSIYC (SEQ ID NO: 4);

SGGRKVFELVGEPSIYC (SEQ ID NO: 5);

CGGRKVFC (SEQ ID NO: 7); and

FELVGEPSIYSTSNDDQVGIWSG (SEQ ID NO: 8).

52. (Four times amended) A process for preparing a**n** **SCR3 derivative** polypeptide **having only a partial SCR3 sequence, wherein the SCR3 derivative polypeptide comprises** **[comprising]** a 6 to 23 amino acid portion of SEQ ID NO: 1, **and** wherein the **SCR3 derivative** polypeptide has at least one amino acid sequence selected from the group consisting of:

(a) amino acids 6-11 of SEQ ID NO: 1, and

(b) amino acids 11-20 of SEQ ID NO: 1**[, and the polypeptide does not comprise a mature short consensus repeat-3]**, comprising the step of: condensing peptide units.

53. (Four times amended) A process for preparing a**n SCR3 derivative** polypeptide **having only a partial SCR3 sequence, wherein the SCR3 derivative polypeptide comprises [comprising]** a 6 to 23 amino acid portion of SEQ ID NO: 1, **and** wherein the **SCR3 derivative** polypeptide has at least one amino acid sequence selected from the group consisting of:

(a) amino acids 6-11 of SEQ ID NO: 1, and

(b) amino acids 11-20 of SEQ ID NO: 1**[, and the polypeptide does not comprise a mature short consensus repeat-3]**, comprising the step of: expressing DNA encoding the polypeptide in a recombinant host cell, and recovering the polypeptide.

54. (Four times amended) An isolated polynucleotide encoding a**n [polypeptide] SCR3 derivative** polypeptide **having only a partial SCR3 sequence, wherein the SCR3 derivative polypeptide comprises [comprising]** a 6 to 23 amino acid portion of SEQ ID NO: 1, **and** wherein the **SCR3 derivative** polypeptide has at least one amino acid sequence selected from the group consisting of:

(a) amino acids 6-11 of SEQ ID NO: 1, and

(b) amino acids 11-20 of SEQ ID NO: 1**[, and the polypeptide does not comprise a mature short consensus repeat-3]**.

55. (Amended) The **isolated** polynucleotide according to claim 54, wherein the polynucleotide is in an expression vector.

56. (Amended) The **isolated** polynucleotide according to claim 54, wherein the polynucleotide is in an expression vector and the expression vector is in a host cell.

57. (Four times amended) A pharmaceutical composition comprising

(1) a therapeutically effective amount of a**n SCR3 derivative** polypeptide **having only a partial SCR3 sequence, wherein the SCR3 derivative polypeptide comprises [comprising]** a 6 to 23 amino acid portion of SEQ ID NO: 1, **and** wherein the **SCR3 derivative** polypeptide has at least one amino acid sequence selected from the group consisting of:

(a) amino acids 6-11 of SEQ ID NO: 1, and

(b) amino acids 11-20 of SEQ ID NO: 1**[, and the polypeptide does not comprise a mature short consensus repeat-3]**, and

(2) a pharmaceutically acceptable carrier or excipient.